taking, and complex investigations make it possible to apply any such principles in a considerable number of cases with a just expectation of success. The exciting work on ferments that has occurred in recent years has greatly transformed the point of view assumed in attacking problems in pathology, but has not in other ways profoundly simplified these problems. The difficulties and complexities have not been essentially lessened; their nature has rather been made more evident.

A BRIEF STUDY OF A DIPHTHERIA EPIDEMIC AT THE ADIRONDACK COTTAGE SANITARIUM (FOR INCIPIENT PULMONARY TUBERCULOSIS).

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Diphtheria epidemics in institutions for the tuberculous are of unusual occurrence, for which reason, as well as on account of the many problems that arise under such conditions, it has been deemed of sufficient interest to report in more or less detail a recent epidemic of diphtheria at the Adirondack Cottage Sanitarium.

The origin of the first case has never been clearly determined. We present the facts as they occurred. Early in October, 1905, one of our orderlies, after a visit to his home, developed a membranous tonsillitis, which on a single culture showed streptococci and no diphtheria bacilli. He was allowed accordingly, after a few days' isolation, to resume his duties. Several cultures taken from his throat at intervals later on during the epidemic, as well as those from his room-mate, were always negative. In the latter part of the month, one of the maids, who had but recently begun work in the laundry and who was with the orderly quite frequently, reported with a well-developed tonsillar diphtheria. She was promptly isolated in her room with her room-mate, her sister, and a strict—as we thought—quarantine established. Later we learned that, standing in her doorway, she would hold conversation with the other maids. After most rigid precautions, including negative cultures, both sisters were discharged, the latter on Saturday evening December 30, 1905. The same day, before the first maid was discharged from quarantine, a patient and one of the maids had a slight soreness of the throat, and two days later when they reported that they felt ill, a second patient went to bed. The second maid, who was employed in the dining-room and linen-room, was at work until she went to bed in the evening, when the diagnosis was made in all three. The patients were isolated and given antitoxin at once. The next day a cottage entirely apart from the other buildings was opened as an isolation pavilion, placed in charge of a competent nurse, and the patients transferred there. The same day, January 2, the throats of all in the institution were carefully inspected, and a patient and two maids with tonsillar membranes were isolated. One of these was probably not diphtheria, although a positive culture was obtained at a later date. The next day, January 3, all patients and employees, irrespective of any pulmonary or other trouble, were given an immunizing dose of 500 units of the antitoxin prepared by the New York State Board of Health. The two cottages and the Childs Memorial, the infirmary where the cases of diphtheria had occurred, were isolated. Each inmate of these cottages was given 1000 units, and not allowed to leave the cottage for one week. During this week several (six) cases of follicular tonsillitis developed, which, we might add, caused much uneasiness, especially as one occurred in one of the infected cottages. The infirmary patients received but 500 units, and one of them who had complained of sore throat developed a membrane on the posterior pillar. She was promptly transferred to the isolation cottage, but the membrane proving by culture to contain only streptococci, she was sent back to the Childs Memorial. It was with some trepidation that immunizing doses were given to five of the infirmary patients, as they were in an advanced stage of tuberculosis, and in three cases the disease was more or less acute. No more cases developed until January 16, two weeks after the first immunizing dose was given, when one of the nurses developed a rather sharp attack of tonsillar diphtheria. The day following, January 17, the fireman, and on January 18 and 19 two patients were attacked. On January 20 a second immunizing dose of 500 units was given to all patients who had not shown especial susceptibility to the antitoxin. To these a dose of 400 units of purified antitoxin prepared by the New York City Board of Health was given a few days later. No more cases of clinical diphtheria developed, but on January 21 it was deemed expedient to take cultures from the throat and nose of every inmate of the institution. The result was appalling, twenty-two of the patients and nine of the employees, including the chef and the baker, revealed positive cultures. The attempt at isolation of inmates with positive cultures, but without clinical symptoms, which had been begun, was gloomily abandoned. The health authorities quarantined the institution, but strange to say few patients became frightened. On January 24 the last case, a patient whose throat was negative at first, developed an apparent follicular tonsillitis which was positive on cultures, and was isolated. A second cottage had been opened and a nurse placed in charge. A third and last immunizing dose (400 units of the purified antitoxin) was given on February 3. The quarantine was raised February 20, after the last case of clinical diphtheria showed two successive negative cultures. No new patients were admitted until February 27, and for some weeks each was given 400 units of antitoxin on admission.

To summarize briefly, the epidemic lasted fifty-one days, that is, from January 2, when three patients became ill, to February 20, when the last patient was discharged from quarantine. Eleven cases of clinical diphtheria developed, and in 32 other individuals diphtheria bacilli were found on culture. There were no fatalities and no serious complications. In all over 400 immunizing doses were given to 174 individuals—129 tuberculous and 45 non-tuberculous.

Epidemics of diphtheria in institutions are by no means rare, but we can find no record of such an epidemic in a sanitarium for pulmonary tuberculosis in which the youngest patient was aged about eighteen years. Such a condition presents many peculiar phases and problems on which we could get little or no information. In the first place, should the patients be given immunizing doses of antitoxin? How often should these doses be repeated? Should cultures be taken from the throat and nose of all the patients or only from those with clinical diphtheria? How should the treatment for the pulmonary tuberculosis be modified, if at all? Should the pulmonary tuberculosis modify the amount of antitoxin in the diphtheria?

The most important point in prophylaxis is complete isolation. We feel now that had we set aside a separate cottage and placed in it the first patient under the supervision of a competent nurse the epidemic would have been avoided. We took every precaution, but it is difficult to impress the necessity of complete isolation upon many persons, not only those of low intelligence. For this reason a nurse is a *sine qua non*. The most careful quarantine was established as soon as the epidemic broke out. No measures were omitted. Every room was carefully fumigated with formaldehyde and completely renovated, and each of the cottages where diphtheria occurred was scrubbed down with corrosive sublimate, revarnished, and retinted.

IMMUNIZING INJECTIONS. All inmates received two or three immunizing doses of antitoxin. The doses were at first 500 and later 400 units.

A small amount of antitoxin prepared by Parke, Davis & Co. was used, but the greater part was from the New York State and City Health Departments.

The injections were made for the most part midway between the scapula and the spines of the eighth and ninth dorsal vertebræ. Many of the women preferred the injection in the arm, but the local reactions were much more severe in that region.

Preparation. The preparation of the skin can be done very simply. It was cleansed with absorbent cotton, usually first with soap and water, then always, and in some cases only, with alcohol. The site of injection was closed with collodion. The most convenient syringe we found to be the small "Sub—Q" glass syringe, with an asbestos wrapped glass plunger, holding about 2 c.c. Small needles were used, and the whole syringe was frequently boiled; after each injection they were rinsed out with boiling water.

Results. In no case did any infection occur. In four instances diphtheria developed between the fourteenth and sixteenth day following the first injection, and in one case four days and in another one day after the second injection. It was therefore deemed advisable, when only 500 units were used, to repeat the injection for two or three times at intervals of two weeks.

The purified antitoxin produced much fewer unpleasant symptoms than the other varieties, which in many instances produced general malaise, more or less rash, swelling of the face, hands, and feet, pain in the joints (so severe in two cases as to cause insomnia and to require morphine), stiffness of the joints, nausea and vomiting, as well as in nearly every case more or less local tenderness and slight swelling for a few hours.

The injections were usually made in the forenoon and the malaise, when present, usually occurred within twenty-four hours. The majority of the patients suffered some slight inconvenience, but in most cases it was of no moment. In some patients it was postponed for eight to fourteen days and occurred simultaneously with the rash.

The rash occurred more in women than in men, and less in the tuberculous than in the non-tuberculous. Of 140 cases, 32 (23 per cent.) had some rash. In 16 cases the rash was severe. The usual form of rash was urticaria, but fine pin-point papules were present in some cases, more often at the site of the injection. A few acne-like papules occurred in a few cases, chiefly on the face and in women. In two patients who had previously suffered from purpura, a crop of purpuric blotches appeared after the injections. No rash occurred after the first or second injections in 92 patients. In 9 it occurred only on the first, in 6 only on the second, and in 4 only after the third immunizing dose. From this it would appear that the rash is as likely to occur after the first as after the second or third injections. Of 10 non-tuberculous individuals the rash appeared on the seventh day in 5, 1 each on the first, second, eighth, and thirteenth days. Among 21 tuberculous cases, the rash appeared as follows: second day, 2; fourth 3; fifth, 1; seventh, 3; eighth, 5; tenth, 5; fourteenth and seventeenth, 1 each. The rash, therefore, occurred more frequently between the seventh and tenth days, but it may occur as early as the first and as late as the seventeenth day after injection.

The pulse was quickened in several patients. One suffered, from palpitation, in another an intermitting pulse was present. The temperature was raised in thirteen patients and possibly more would have shown this symptom had careful records been kept of each patient. In no instance was the temperature raised for more than a few days. In three patients who were in bed on account of elevated temperature the injections produced no noticeable effect on the temperature further than to raise it a fraction of a degree for a few hours. Stiffness in the joints of the hands, knees, and in several instances in the hips, was present. Associated often with the stiffness and possibly its cause in some instances was swelling of the face, hands, and feet. In many cases the swelling was more or less localized in the arm or leg where the injection was made. Marked swelling occurred in thirteen cases.

The axillary glands were enlarged in five cases in which the injections were made in the back. In one case a chain of enlarged and tender glands extended to the breast. Diarrhœa occurred in one case, chills in another, and pleurisy in a third. In two cases, hemoptysis occurred about one week after an immunizing dose. In some of the foregoing instances the "complications" were no doubt mere coincidences and we believe this to be true more especially of the hemoptyses.

THERAPEUTIC INJECTIONS. The tuberculous were treated when they developed diphtheria, exactly as the non-tuberculous; but when possible they were placed in bed out-of-doors and they slept and lived in rooms with windows wide open at all times. The antitoxin was given in doses of 2000 units daily in the thighs until the symptoms and membrane were markedly affected. In three patients no rash developed, but one, a tuberculous patient, had besides the two immunizing doses of 500 units only one large dose, 4000 units. The rash in the other eight was urticarial, severe and general in six, confined to the legs in two.

One patient, a non-tuberculous case, had some cardiac weakness, but no other complications occurred. The patients, with but two exceptions, received large doses on the first day of the appearance of symptoms, when the membrane was wholly confined to the tonsils. The membrane disappeared in two non-tuberculous cases in five and seven days, in five tuberculous cases, in three, three, five, six, and seven days respectively.

No immediate effect upon the tuberculous process was noted in any cases. The fever disappeared as quickly as in the non-tuberculous. The cough was not increased nor did any patient have night sweats or hemoptyses, though an occasional pleuritic pain was complained of, which, however, was not out of the ordinary. A careful examination of the lungs a short while after discharge from quarantine revealed in all cases an improvement, more or less marked, in the pulmonary condition.

CONCLUSIONS. From our experience in this mild diphtheria epidemic we would conclude that:

1. In institutions immunizing doses of antitoxin of 500 units should be given every two weeks for two or three times.

2. Diphtheria may occur in patients two weeks after an immunizing dose of 500 units.

3. It is unnecessary to endeavor to separate individuals with positive cultures from the nose or throat without clinical symptoms from those with negative cultures when immunization is carried out.

4. One negative culture from the throat is sufficient neither for diagnosis nor for raising quarantine.

5. The advisability of taking cultures from the nose except in nasal diphtheria may be questioned.

6. Careful isolation for three or four weeks under a trustworthy nurse should be practised. After that time the patient with a positive culture should be kept out of the general dining-room or buildings and at a distance of four feet from all non-diphtheritic patients.

7. Some untoward symptoms, usually slight, appear in most patients. A rash, arthralgia, swelling, and general malaise occur most frequently. Slight transitory rise of temperature occurs frequently.

8. In institutions where the out-door treatment is rigidly enforced the epidemic will probably be cut short.

9. In the presence of a diphtheria epidemic, patients with pulmonary tuberculosis should be treated as regards the diphtheria as otherwise healthy individuals.

10. When the tuberculous contract diphtheria they should be moved out-of-doors as soon as possible.

11. Mild diphtheria seems to exert little or no harmful influence upon the pulmonary lesion in the tuberculous.

12. The antitoxin in small or large doses seems to have little or no effect upon the pulmonary tuberculosis.

13. Immunizing doses may be given to patients with fever.

14. Complications seem to occur after diphtheria no more often, possibly less, in the tuberculous than in the non-tuberculous.

We desire to record here our hearty appreciation of the kindness of the officers of the New York State and City Boards of Health. We feel that it is but just to say that without their assistance and advice and the promptness with which they supplied us with antitoxin this mild epidemic might have been most serious. Our acknowledgments are due also to the health authorities of the village of Saranac Lake and of the township of St. Armand.